

REMARKS

Oath/Declaration

The Office Action objected to the Oath/Declaration because of informalities.

Applicants are submitting herewith a substitute Oath/Declaration. Withdrawal of the rejection is respectfully requested.

Status of the Claims

Claims 1-116 were previously cancelled. Claims 126, 133, 138, 139, 142, 143 and 149-178 were previously withdrawn. Applicants respectfully reserve the right to pursue the non-elected subject matter in one or more continuation, continuation-in-part, and/or divisional applications pursuant to 35 U.S.C. §§ 120 and 121. Claims 117-125, 127-132, 134-137, 140, 141 and 144-148 are currently pending.

Claim Rejection— 35 U.S.C. § 112 ¶ 2

Claims 17, 117-125, 127-132, 134-137, 140, 141, and 144-148 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Examiner states that the newly added limitation “wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide nucleotide” is new matter. The Examiner further states that Applicants did not indicate those portions of the specification that support the amendments.

Applicants respectfully direct the Examiner’s attention to the paragraph entitled “Claim Amendments” on page 13 of the Response dated November 17, 2006. Support for the above-mentioned amendments may be found at page 6, lines 19-32; page 8, lines 27-33; and page 19, lines 17-26 of the originally filed specification. Withdrawal of the rejection is respectfully requested.

Claim Rejection— 35 U.S.C. § 102(e)

Claims 117-119, 121, 125, 134-136, 144 and 145 were rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,214,136 (“*Lin et al.*”). Applicants respectfully disagree and traverse this rejection.

The present invention of claim 117 is drawn to a nucleic acid displacer composition comprising an isolated single-stranded oligo-or polynucleotide displacer comprising two or more sequences wherein at least one second sequence comprises one or more modified nucleotides which are different and one or more nucleotides that form a mismatch with the receipt polynucleotide, wherein said displacer changes at least one nucleotide or nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. Since “[a]nticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention.” Electro Med. Sys. S.A. v. Cooper Life Sciences, 32 U.S.P.Q.2d 1017, 1019 (Fed. Cir. 1994), Applicants respectfully submit that *Lin et al.* fails to meet the limitations of the instant claims.

Lin et al. describes oligonucleotide sequences modified by conjugation to at least one substituted or unsubstituted anthraquinone. *Lin et al.* claim that the oligonucleotides enhance hybridization to target DNA or RNA without loss of specificity and enhanced stability to nucleases. Col. 2, lines 26-34.

In contrast, the instant claims are drawn to a nucleic acid displacer composition comprising an isolated single-stranded oligo-or polynucleotide displacer wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. This differs from *Lin et al.* in that the claimed oligo-or polynucleotide displacer changes at least one nucleotide or nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. While the Office Action asserts that the “displacer” of *Lin et al.* “changes at least one nucleotide or nucleotide sequence in the receipt polynucleotide”, Applicants can not find support for this in *Lin et al.* Office Action at 5.

It appears that the Examiner is referring to Example 5, “Specificity of Hybridization” for support that *Lin et al.* teach that the displacer changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide when the displacer is introduced into the recipient

polynucleotide. Col. 9, line 9 through Col. 10, line 15. However, a closer reading of this section gives no indication that the displacer changes a nucleotide in the recipient polynucleotide. Here, the oligomers containing the anthraquinone-conjugated polynucleotides were evaluated with regard to hybridization specificity as compared to controls (oligomers which do not contain the anthraquinone). The anthraquinone-conjugated polynucleotide oligomer (which the Examiner has labeled a “displacer” and contains a mismatch) are complexed to a single-stranded RNA molecule. The authors then measured the changes in melting temperatures caused by the single base-pair mismatch in the *oligomer*, as opposed to the single-stranded RNA molecule (recipient polynucleotide). There is no indication in Example 5, or anywhere else in the reference, that Lin *et al.* teaches or contemplates a displacer that changes a nucleotide in the recipient polynucleotide. Each and every limitation of independent claim 117, and the claims depending from claim 117, is not taught or suggested by the cited reference.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejection— 35 U.S.C. § 103

Claims 146 and 147 were rejected under 35 U.S.C. § 103(a) as unpatentable over Lin *et al.*, as applied above, and further in view of US Patent No. 5,260,433 (“Dattagupta”). Applicants respectfully disagree and traverse this rejection.

A proper obviousness rejection of patent application claims under 35 U.S.C.

§ 103(a) requires a showing by the USPTO that the invention defined in the rejected claim(s) as a whole is obvious in view of one reference or a combination of the references. M.P.E.P. § 2142. Three basic criteria must be met to support a *prima facie* case of obviousness: (a) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference(s) teachings; (b) there must be a reasonable expectation of success; and (c) the prior art reference (or references when combined) must teach or suggest all the claim features. M.P.E.P. § 2143. Here, the references cited in the Office Action do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants’ claims 146 and 147.

Applicants respectfully note that “Dattagupta” was incorrectly cited as “5,260,433” in the Office Action but correctly listed on the PTO-892 form.

The Examiner characterizes Lin *et al.* as above. The Office Action noted that the differences between Lin *et al.* and the claims are that Lin *et al.* does not disclose:

that said modification in claim 144 is selected from the group consisting of biotin moieties, phosphorothiate linkages and antigens as recited in claim 146 and a modification which allows capture of the displacer-recipient complex by affinity chromatography as recited in claim 147. Office Action as page 7.

To fill this gap, the Office Action asserts that Dattagupta *et al.* discloses that

a nucleic acid probe can be labeled with hapten or biotin, an enzyme such as β -galactosidase or horse radish peroxidase, a fluorescent radical, a phycobiliprotein, a luminescent radical, or a radioisotope (see abstract) and that it is known that biotin binds to avidin. Office Action at 7.

The Office Action concluded that one of ordinary skill in the art would have found it obvious to have made the displacer recited in claims 146 and 147 with the modification being biotin to allow capture of the displacer-recipient complex by affinity chromatography. Office Action at 8. The Office Action asserted that one of ordinary skill in the art, “would have been motivated to do so because the replacement of one type of label (fluorescent as taught by Lin *et al.*) with a different type (biotin as taught by Dattagupta *et al.*) would be obvious because the labels are used for the same purpose (the labeling of a nucleic acid probe), Office Action at 8. The Office Action also asserts that one of ordinary skill in the art would have had a reasonable expectation of success because the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Office Action at page 8.

As discussed above, Lin *et al.* does not disclose the instantly claimed displacer that changes a nucleotide in the recipient polynucleotide.

Applicants submit that the references cited in the Office Action do not individually or in combination suggest to a person of ordinary skill in the art the invention of the Applicants’ dependent claims 146 and 147, which incorporate all of the elements of independent claim 117.

The Office Action fails to establish why or how it would have been obvious to one of ordinary skill in the art at the time of the invention to combine Lin *et al.* with Dattagupta *et al.* to produce an oligo- or polydeoxynucleotide displacer meeting all the limitations of claims 146 and 147.

Even if, *arguendo*, it were proper to combine the references, it has not been established in the Office Action that the combination would have yielded a composition that meets each and every limitation of the claims. The Dattagupta *et al.* reference does not cure the deficiencies of Lin *et al.* Dattagupta *et al.* discloses a labeled nucleic acid probe for detection in hybridization assays and for the determination of specific polynucleotide sequences. See Abstract. The probe is labeled by means of photochemistry and employs a photoreactive nucleic acid binding ligand. Col 1, lines 39-54. Nowhere does Dattagupta *et al.* teach the displacer molecule of Applicants' presently claimed invention. The Lin *et al.* modified oligonucleotide sequences are distinct. Absent an explicit teaching or a suggestion in Lin *et al.*, it would not have been obvious to a person of ordinary skill in the art to modify the oligonucleotide sequences described therein. Thus, a person of ordinary skill in the art would not have found it obvious to combine the teachings of the cited references because neither Lin *et al.* nor Dattagupta *et al.* teaches each and every limitation of the claims. The improper combination of the references fail to suggest to a person of ordinary skill in the art the use of the oligonucleotide sequences of Lin *et al.* to produce the isolated single-stranded oligo-or polynucleotide displacer wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide. as required by claim 117.

In addition, the Examiner is incorrectly describing the use of labels by Lin *et al.* Lin *et al.* does not disclose DNA probes. The anthraquinone is used as an agent to increase stability, not as a label. In fact, the detection of anthraquinone is not described at all. There is no evidence that the derivative use of anthraquinone has fluorescent properties that would enable it to be used as a label for detecting DNA-DNA hybridization.

To establish a *prima facie* case of obviousness of a claimed invention, the Office Action must establish that each limitation of the rejected independent and dependent claims is taught or suggested by the prior art. M.P.E.P. § 2143.03. The Office Action failed to do so at least

because no evidence was presented that prior art teaches or suggests all limitations of the rejected claims.

Reconsideration and withdrawal of the rejection is respectfully requested.

As stated above, Applicants believe that that “Dattagupta” was incorrectly cited as “US Patent No. 5,260,433” in the Office Action but correctly listed on the PTO-892 form. US Patent No. 5,260,433 corresponds to Engelhardt *et al.* In the event that the current rejection was directed towards Engelhardt *et al.*, Applicants respectfully submit that this rejection is also improper. The instant application is assigned to Enzo Biochem, Inc. and Engelhardt *et al.* is assigned to Enzo Diagnostics, Inc. Enzo Biochem, Inc. and Enzo Diagnostics, Inc. are commonly owned and therefore Engelhardt is not a valid reference pursuant to 35 U.S.C. § 103(c). Included with this Response is a copy of the Statement of Common Ownership pursuant to M.P.E.P. § 706.02(l)(2) previously submitted with the Amendment and Response filed November 17, 2006. Therefore, it is legally improper to combine Lin *et al.* with Engelhardt *et al.* for purposes of an obviousness rejection under 35 U.S.C. § 103(a).

Claim 148 was rejected under 35 U.S.C. § 103(a) as unpatentable over Lin *et al.*, as applied above. The Office Action asserts that Lin *et al.* “does not disclose an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybrid to the nucleic acid displacer composition of claim 118.” Office Action at page 9. Applicants assume that the Examiner is referring to claim 148. The Examiner further states that it would have been obvious to have made the naturally occurring recipient polynucleotide duplex hybrid by hybridizing the nucleic acid displacer composition to a naturally occurring RNA. Office Action at page 9. The Examiner contends that one having ordinary skill in the art would be motivated to combine the references because Lin *et al.* discloses experiments in which the oligonucleotide coupled to anthraquinone is hybridized to a single stranded RNA. Finally, the Examiner concludes that a person of ordinary skill in the art would have a reasonable expectation of success to make the artificially constructed polynucleotide. Office Action at page 9.

Applicants respectfully traverse the rejection. As discussed above, Lin *et al.* does not describe the instantly claimed oligo- or polynucleotide displacer meeting all the limitations of dependent claim 148, which incorporates all of the elements of independent claim 117. Specifically, Lin *et al.* does not teach a displacer that changes a nucleotide in the recipient

polynucleotide. Thus, there would be no motivation to alter the Lin *et al.* displacer to form an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybrid to the nucleic acid displacer composition. There would be no expectation of success because the altered composition would not result in Applicants presently claimed invention.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants respectfully submits that claims are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any patentability issues remain after consideration of this Response, the Examiner is invited to contact the Applicants' undersigned representative to discuss and resolve such issues.

In the event that a variance exists between the amount tendered and that deemed necessary by the U.S. Patent and Trademark Office to enter and consider this Response or to maintain the present application pending, please credit or charge such variance to the undersigned's **Deposit Account No. 50-0206**.

Respectfully submitted,

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